Influence of nutrition and management on eggshell quality

Conference report

Many factors affect eggshell quality, such as nutrition, disease, genetics, environmental conditions, age of birds, stress, egg collection and handling, and packaging and transport. Eggshell quality, however, is primarily related to management and nutrition, not genetics or other factors. It is becoming a bigger issue as the length of the laying period has extended because, as hens get older, shell quality drops.

“The information in the genetics companies’ management guides is for direction and information only, as each egg producer’s production goals and conditions can vary”, says Vitor Arantes, Global Technical Services Manager and Global Nutritionist, Hy-Line International. He advises listening to your birds. For example, “diets should be aligned with the bird’s bodyweight development, rather than the age of birds and following feeding phases according to pre-planned timings for feed changes,” he noted.

Below are some of the nutritional factors impacting eggshell quality that producers should keep top of mind.

Early development and pre-starter diets

“Bodyweight at 6-12 weeks of age is key, but to achieve this goal, bodyweight up to 5 weeks of age is a MUST, stressed,” Dr. Arantes. “This critical period is an investment, so don’t be shy. Poor management in the first 5 weeks will delay production, increase mortality, and prevent the achievement of peak production targets. In turn, it will affect egg quality. Therefore, we must provide proper diets as soon as possible,” he said.

As shown below, chicks hatch with relatively underdeveloped internal organs and systems. During the first 5 weeks of age, the digestive tract and the immune system undergo much of their development. The development of the intestine is crucial for nutrient absorption and will determine a hen’s future production efficiency. Strong intestinal development will also strengthen the immune system and reduce the

possibility of future enteric diseases and improve the response to vaccinations.

Multi-phasic body weight development during rearing and the start of lay

Pre-starter diets support the chicks' transition from being fed by the yolk sac and are relatively high in energy, protein, and the vitamins and minerals required for growth and development. The chicks' limited digestive capacity post-hatch demands easily digestible raw materials. A crumble containing high-quality, functional ingredients provides a good nutritional start in life. The use of feed additives, such as enzymes to improve digestibility, and synbiotics to aid in the early development of a microbial population and to prevent the intestinal colonization of pathogens, known as competitive exclusion, should be considered.

Teaching hens how to eat – preparing for the pre-peak phase

The objective is to develop sufficient feed intake capacity for the period start of lay, by feeding a developer diet from 10-16 weeks of age. This is a diluted diet with high levels of insoluble fiber to develop feed intake capacity (crop and gizzard).

"You can train pullets to eat by taking advantage of their natural feeding behavior," commented Dr. Arantes "Because birds consume most of their feed before lights go off, the main feed distribution (60% of the daily ration) should be in the late afternoon, about 2-3 hours before 'light off'. In the morning, birds will be hungry and finish the feed, including fine particles. Emptying feeders helps to prevent selective eating and will increase the uniformity of the flock. In the middle of the day, there should be no feed in feeders for 60-90 minutes," he noted.

Don't neglect the pre-lay phase

Start feeding a pre-lay diet when most pullets show reddening of the combs, which is a sign of sexual maturity. Feed for a maximum of 10–14 days before the point of lay. This is important to increase medullary bone calcium reserves. Large particle calcium should be introduced in this phase. Do not feed pre-lay later than the first egg as it contains insufficient calcium to support egg production.

There can be a negative impact on feed consumption from the sudden increase in dietary calcium levels from 1% to above 4% at the start of lay. Field experience indicates that the use of pre-lay diets helps as a smooth transition between the developer (low calcium and nutrient density) and the peaking diet. Correct feed formulation and matching diet density with consumption will minimize the impact of reduced calcification of bone over the laying cycle and extend the persistency of shell quality. It also helps to avoid the often-reduced appetite/daily feed intake during early production.

The following are suggested for pre-layer feed:

- 1.25 to 1.40% P
- 2.5% Ca (50% coarse limestone)
- 900-1,100g per hen total
- Never before 15 weeks of age
- Never after 2% hen day (HD) egg production

Understand your limestone

Calcium particle size is important for eggshell quality. Fine calcium carbonate particles pass through the gastrointestinal tract in 2-3 hours, whereas particles above 2mm are retained in the gizzard and will slowly solubilize, delaying the calcium assimilation. Eggshell formation takes 12 to 14 hours and occurs mainly during the night period. Providing a high amount of large calcium particle size before the night, when birds are sleeping, will help laying hens to produce a strong eggshell.

The ratio of coarse to fine calcium particles will increase with bird age as below. Changing the particle size ensures that more calcium will be available at night from the diet instead of from the bone.

Calcium particle size recommendations

Particle size	Starter, Grower, Developer	Pre-Lay	Weeks 17-37	Weeks 38-48	Weeks 49-62	Weeks 63+
Fine (<2mm)	100%	50%	40%	35%	30%	25%
Coarse (2-4mm)	–	50%	60%	55%	70%	75%

The solubility of limestone may differ according to the source. Calcium with high solubility will not be stored for a long time in the gizzard, negating the particle size effect. Dietary calcium levels may need to be adjusted based on the solubility of your limestone. The in vitro solubility of your limestone source can easily be checked on the farm, with a simple technique using hydrochloric acid. The target is to recover 3-6% of the supplemented limestone.

Water

It’s impossible to have good eggshell quality if you don’t have good water intake and good quality water. For example, excessive salt levels in drinking water can cause persistent damage to shell quality.

Conclusion: invest in the rearing phase

Good nutrition and management practices are key to good shell quality. The rearing period is a key developmental time for future success during the laying period – it is an investment phase.

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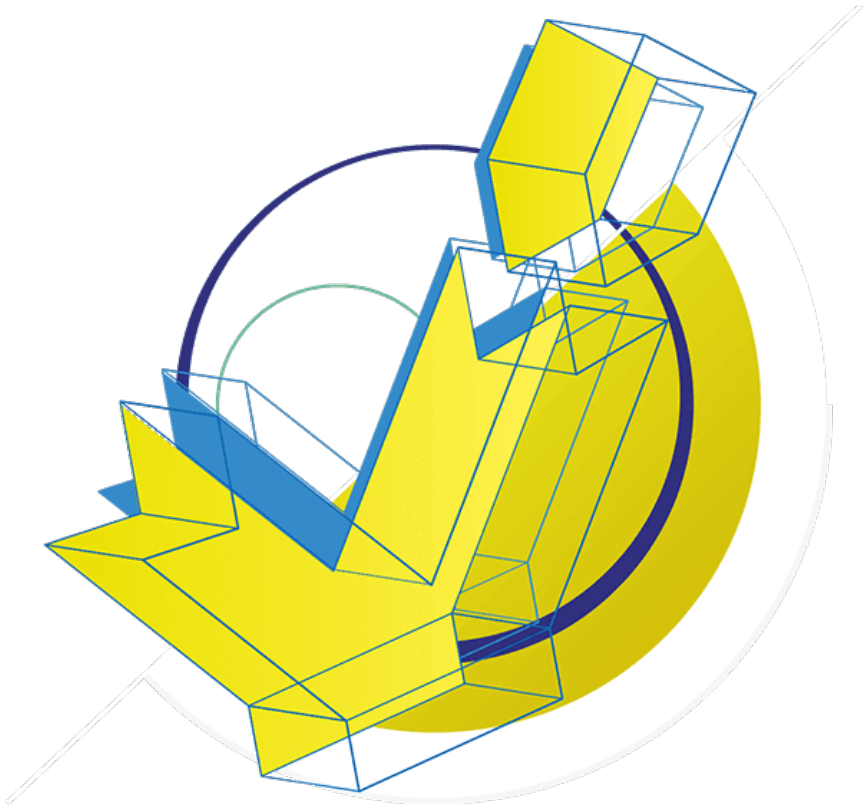
EW Nutrition’s Poultry Academy took place in Jakarta and Manila in early September 2023. Vitor Arantes, Global Technical Services Manager and Global Nutritionist, Hy-Line International, was a distinguished guest speaker in this event.

Gustavo Tesolin appointed Regional Director of EW Nutrition LATAM



Gustavo Tesolin

29 January 2024, Visbek – German-based company EW Nutrition, a global provider of functional animal nutrition solutions, has appointed Gustavo Carlos Tesolin as its Regional Director for Latin America.

An agricultural engineer by training, Gustavo Tesolin has forged an international career in the Animal Health business during the last 25 years. With different leadership roles in several major international organizations such as Novartis, Elanco, and Erber Group, Mr. Tesolin brings along important experience in Commercial Operations, P&L drive, and Strategy execution, with special emphasis on team development and geographic expansion.

“I am really excited to join a company as innovation-driven and science-focused as EW Nutrition,” Tesolin said. “The recent launch of VENTAR D, a novel phytogenic specifically designed and developed to improve animal husbandry results, will continue to strengthen our position in the region, together with our winning brands PRETECT D and ACTIVO” and added, “I am eager to take on the challenge and better acquaint the market with an excellent portfolio centered on Gut Health Management, Digestibility, and Feed Quality.”

Jan Vanbrabant, CEO of EW Nutrition, noted that Gustavo Tesolin is “the perfect combination of the right experience and the right attitude. We are happy to have found in him a proven leader with not just

excellent market knowledge, but with the same values we share in EW Nutrition: a passion for innovation in the service of our customers, and relentless curiosity and energy to find the right solution.”

This appointment comes on the heels of several top-tier global hires over the last 18 months and reflects the company’s commitment to the Latin American market.

Tesolin will move to Mexico to coordinate EW Nutrition’s expansion in Latin American countries.

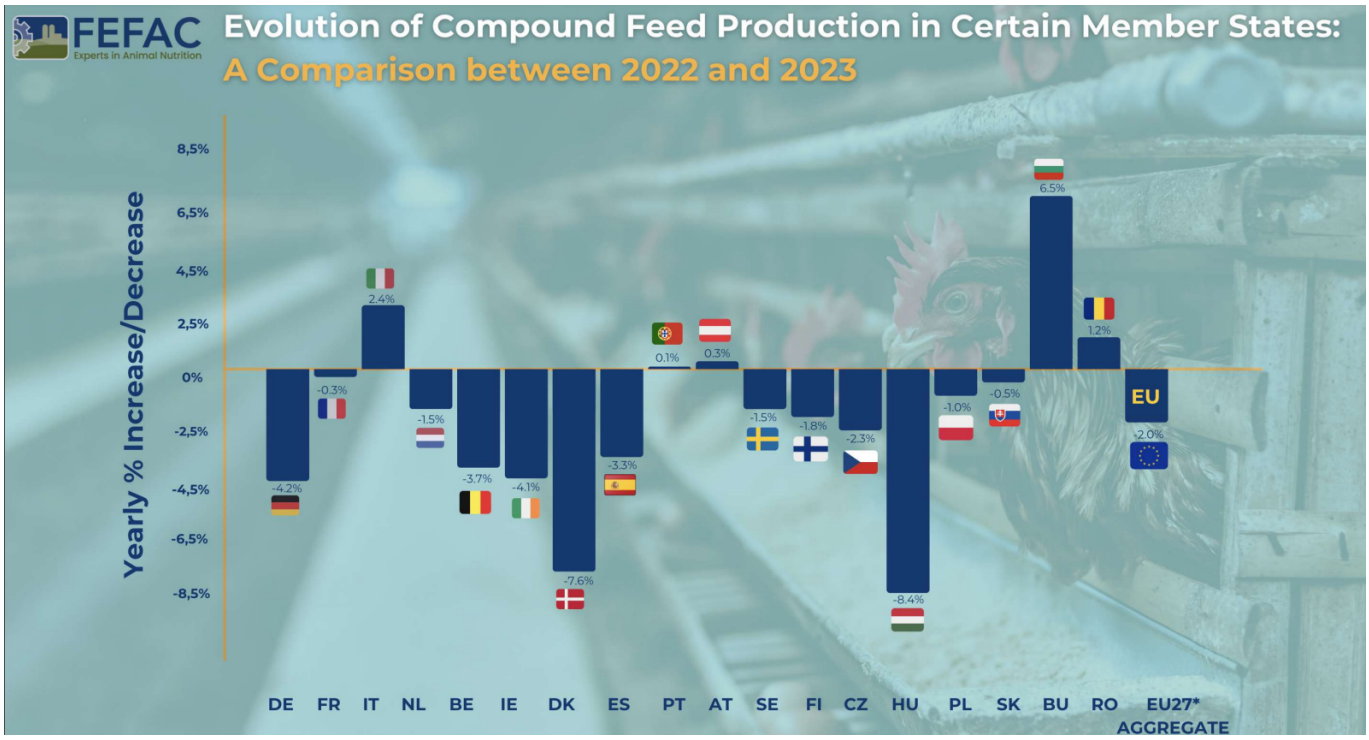
About EW Nutrition

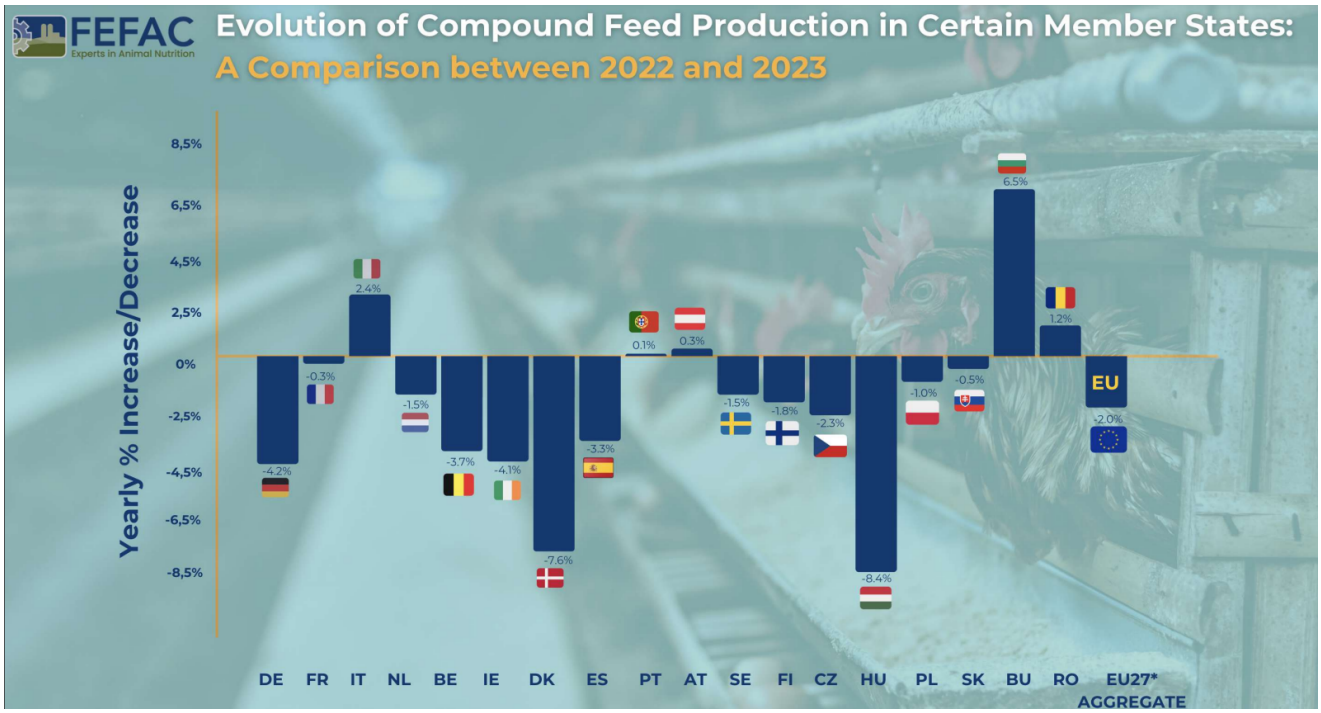
EW Nutrition is a German-based international animal nutrition company that offers comprehensive solutions for animal gut health, toxin risk management, growth performance, and more.

Press contact

marketing@ew-nutrition.com

FEFAC: Quick Overview of 2023 EU Compound Feed Production





Total Production 2023: 144.3 million metric tons for farmed animals

Change from 2022: 2% decrease

Factors Influencing Decrease

Political and Market Pressures: Addressing crises and the shift towards sustainable feed.

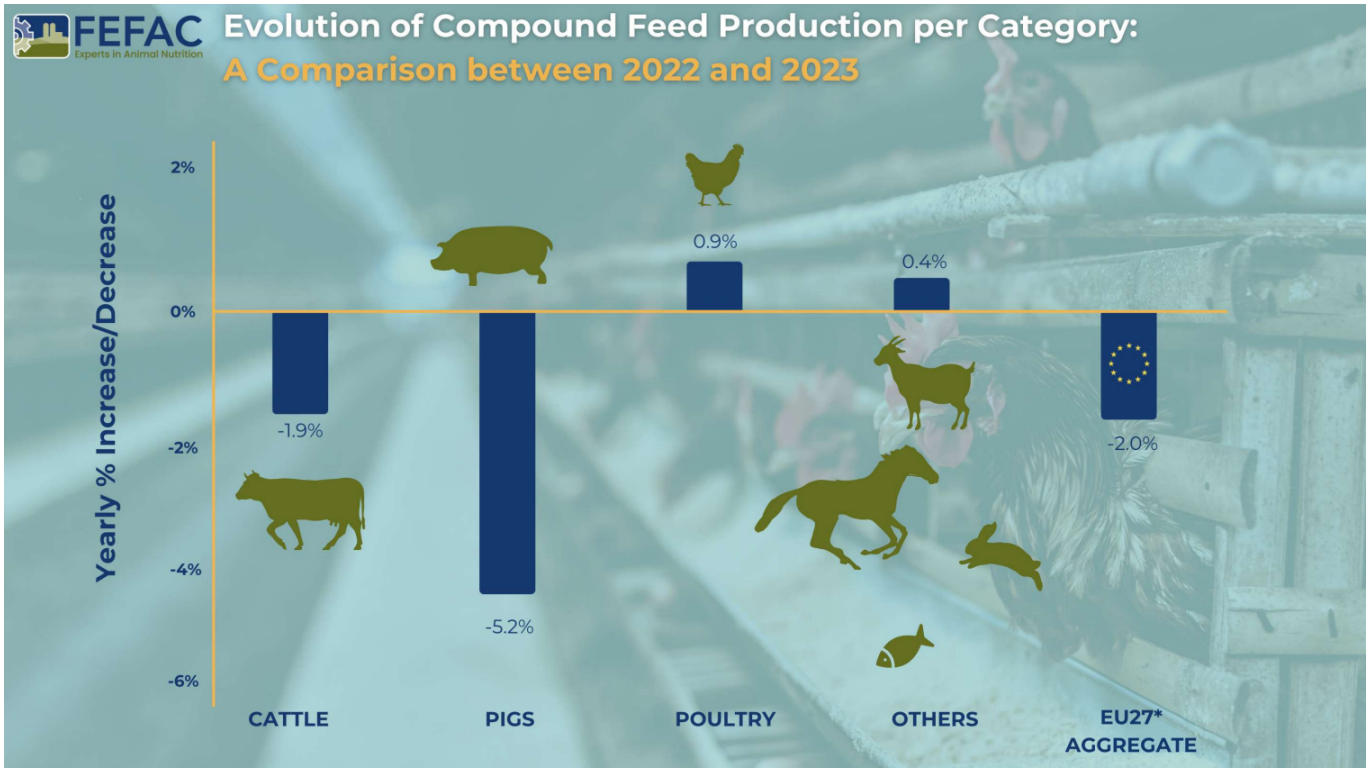
Climate and Diseases: Effects of droughts, floods, Avian Influenza (AI), and African Swine Fever (ASF) on raw material supply and animal production.

National Policies: Initiatives for greenhouse gas and nitrate emission reduction.

Consumer Trends: Food price inflation impacting demand.

Production Variability: Different trends across EU Member States, with notable decreases in countries like Germany, Ireland, Denmark, and Hungary, and slight increases in Austria, Bulgaria, Italy, and Romania.

Sector-Specific Trends



By Species

Pig Feed: Major decline of nearly 2.5 million tons. Key challenges included:

- Loss of export markets, particularly in Asia
- Negative media impact in Germany
- Significant production drop in Denmark (-13.6%) and Spain (loss of 800,000 metric tons)
- Italy's ongoing struggle with ASF

Poultry Feed: Increase by 0.9 million tons, yet still 700,000 metric tons below 2021 levels. Challenges included declines in Hungary and Czechia due to reduced broiler production.

Cattle Feed: Decrease of 0.8 million tons from 2022.

2024 key factors

- Animal disease
- Economic instability, persistent food price inflation
- Weather irregularities
- Continued imports of poultry meat from Ukraine
- "Green and animal welfare" policies affecting local production

Summary

The EU's compound feed production in 2023 faced numerous challenges, leading to an overall decrease. The pig feed sector was most severely hit, while poultry feed showed some recovery. The influence of environmental, economic, and policy factors played a significant role in shaping these trends. Despite the price of feed cereals falling back to the levels seen before Russia's invasion of Ukraine, these challenges will continue to be felt in 2024.

Source: FEFAC

EW Nutrition welcomes Jan Vanbrabant as new CEO

VISBEK (Germany), 1 September 2023 — EW Nutrition, a leading global provider of functional animal nutrition solutions, welcomes Jan Vanbrabant as its new Chief Executive Officer.

Jan has a PhD degree in microbiology and is an experienced manager in animal health and nutrition, having held leadership roles at DSM, Erber Group, Biomin and Kemin.

“We are very pleased that we have found a strong management lead in Jan, who embodies the philosophy of EW Nutrition”, says Jan Wesjohann, Managing Director of parent company EW Group. “EW Nutrition is an innovation-driven company, with intensive investment in R&D. Together with Jan we are looking to enter the next growth phase of EW Nutrition.”

“I am very excited to be joining the EW Nutrition team,” said Jan Vanbrabant. “EW Nutrition’s long-term focus has created an extremely competitive portfolio. EW Nutrition is uniquely positioned to support its customers in mastering the challenges of the changing animal health and nutrition environment.”

Former CEO Michael Gerrits is heading into retirement after six years leading EW Nutrition. “I want to thank Michael Gerrits for his essential stewardship in bringing the company to the next level,” said Jan Wesjohann.

About EW Nutrition

EW Nutrition is a global animal nutrition company that offers integrators, feed companies, and veterinarians comprehensive solutions for animal gut health and performance, feed quality, digestibility, and more. It is focused on promoting sustainable growth through reduced FCR, natural support against challenges, reduced need for antibiotics, and planet-friendly protein production.

Contact:
Ilinca Anghelescu
marketing@ew-nutrition.com

Cryptosporidia in calves – chickens can help

*By **Lea Poppe**, Regional Technical Manager, EW Nutrition*

Diarrhea due to infestation with cryptosporidia is one of the most pressing problems in calf rearing. These protozoa, along with rotaviruses, are now considered the most common pathogens in infectious calf diarrhea. Due to their high resistance and thus limited possible control and prevention measures, they have now overtaken other pathogens such as coronaviruses, salmonellae, and *E. coli*.

Cryptosporidia show complex development

Cryptosporidia are single-celled intestinal parasites. In calves, Cryptosporidium parvum and Cryptosporidium bovis are most commonly found. C. bovis is normally considered nonpathogenic. Accordingly, the disease known as cryptosporidiosis is caused by C. parvum. The rapid tests for determining the diarrheal pathogens, which are increasingly widespread, are usually unsuitable for distinguishing between the individual strains, which can lead to false positive results.

Resistant in the environment, active in the

animal

In the environment, cryptosporidia are distributed as oocysts. The oocysts are only about 5 µm in size and have a very resistant shell. They can remain infectious for up to 6 months in high humidity and moderate temperatures. Drought and extreme temperatures (below -18°C and above 65°C) cause the oocysts to die.

After oral ingestion, the oocysts are reactivated by conditions in the gastrointestinal tract (low pH and body temperature): As sporozoites, the parasites attach to the posterior small intestine, causing diarrhea symptomatology. There, they surround themselves with a special protective membrane, and the complex life cycle continues. Only a few days after infection, reproductive forms are detectable in the calf's intestine, and excretion of infectious oocysts in the feces begins.

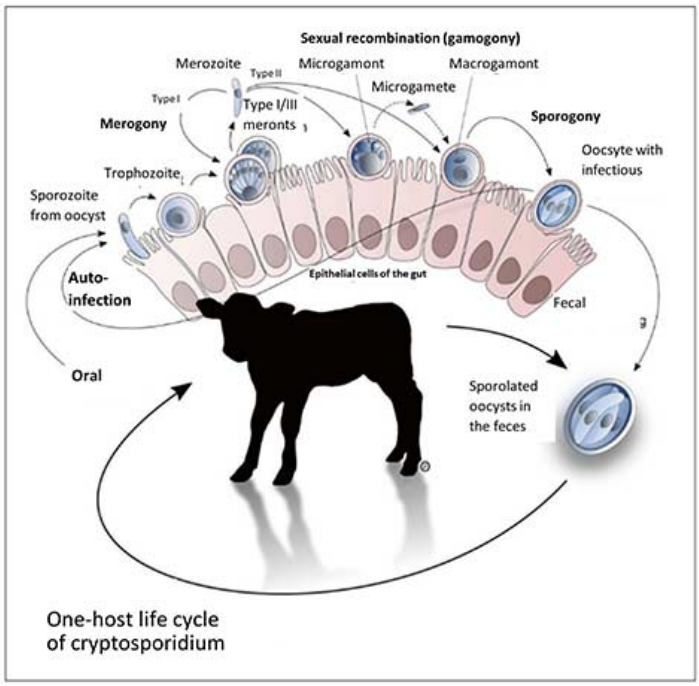


Figure 1 (Olias et al., 2018): Life cycle of cryptosporidia: ingested oocysts release four sporozoites that invade host enterocytes (intestinal epithelial cells). There, they develop into trophozoites before asexual and sexual reproduction ensues, and thin- and thick-walled oocysts are formed. Thick-walled oocysts are excreted through the intestine. Thin-walled oocysts may break apart, and the sporozoites may infect other enterocytes, resulting in relapse or prolonged diarrhea. Infestation of the cells leads to their destruction, resulting in villi atrophy or fusion.

Oocysts bring the disease to the animal

Cryptosporidiosis is transmitted either by direct contact of calves with feces from infected animals or indirectly by ingesting contaminated feed, bedding, or water. Each gram of feces excreted by calves showing symptoms may contain up to 100 million oocysts. According to experimental studies, as few as 17 orally ingested oocysts are sufficient to trigger infection. In addition, some multiplication forms can infect other intestinal cells directly within the intestine and thus further advance the disease by autoinfection.

Cryptosporidiosis caused by cryptosporidia often presents with typical diarrhea symptoms and occurs primarily in calves up to 3 weeks of age. Older calves may also be infected with cryptosporidia but usually show no symptoms. Pathogen excretion and, thus, the spread of disease within the herd is nevertheless likely due to the minimal infectious dose.

Damage to the intestinal wall leads to

retardation of growth

Attachment of cryptosporidia to the intestinal wall is associated with an inflammatory reaction, regression and fusion of the intestinal villi, and damage to the microvilli. As a result, nutrient absorption in the small intestine is impaired, and more undigested nutrients enter the colon. The microflora starts a fermentation process with lactose and starch, leading to increased lactate levels in the blood and, thus, hyperacidity in the calf. Faintness, unwillingness to drink, recumbency, and growth disorders are the consequences.

Diarrhea often occurs late or not at all and, accordingly, is not considered the main symptom of cryptosporidiosis. When diarrhea occurs, it lasts about 1-2 weeks. The feces are typically watery, greenish-yellow, and are often described as foul-smelling. Due to diarrhea, there is a loss of electrolytes and dehydration.

Studies show: Cryptosporidia are the most prevalent diarrheal pathogens

Several studies in different regions, which examined calf diarrhea and its triggers in more detail, came to a similar conclusion: Cryptosporidia are one of the most common causes of calf diarrhea. In addition, mixed infections often occur.

Country or region	Number	Age/Health status	% Crypto-sporidia	% Rota viruses	Combined infections with crypto-sporidia	Others (%)	Source
Switzerland		2 – 21 DL Ill and healthy	43	46		1 case of E. coli	Luginbühl et al., 2012
Switzerland	63	1 – 4 DL Ill and healthy ———– 7 – 20 DL ———– 26 – 49 DL	34.4 ———– 54.0 ———– 33.3	3.1 ———– 28.6 ———– 13.3	2 EP – 1.6 4 EP – 3.2 ———– 2 EP – 19 3 EP – 3.2 4 EP – 0 ———– 2 EP – 30 3 EP – 11.7 4 EP – 6.7	Corona 4.7 E. coli 4.7 Giardia 1.6 ———– Corona 0 E. coli 3.2 Giardia 6.3 ———– Corona 0 E. coli 15 Giardia 35	Weber et al., 2016 Weber et al., 2016 EN
Switzerland	147	Up to 3rd WL; Diarrhea	55	58.7		5.5 % Rota 7.8 % BCV	Lanz Uhde et al., 2014
Sweden	782	1 – 7 DL Diarrhea	25.3		Detected with Giardia, E. coli, Rota, Eimeria		Silverlås et al., 2012
USA (East coast)	503	Pre-weaning	50.3				Santin et al., 2004
USA	30	2 weeks old 1-8 weeks old 3-12 months 12-24 months	96.7 45.8 18.5 2.2				Santin et al., 2008
Germany	521		32	9			Losand et al., 2021
Ethiopia	360		18.6				Ayele et al., 2018
Argentina	1073	n.m. / Ill and healthy	25.5				Lombardelli et al., 2019
UK	n.m.	Ill ??	37	25	20	Coccidia 8 E. coli 4 Corona 3 Co infections not including Crypto-sporidia 3	APHA, SRUC, Veterinary investigation diagnosis analysis (VIDA) report (2014)

DL = days of life WL = weeks of life n.m. = not mentioned EP = enteropathogen

Cryptosporidia reduces profit

Infection with cryptosporidia and sometimes subsequent diarrhea entails treatment of the animals and generates costs (veterinarian, medication, electrolyte drinks). In addition, poorer feed conversion, lower growth, and animal losses result in lower production efficiency.

A Scottish study shows 34 kg less gain in the first six months of life compared to healthy calves in beef calves that experienced severe cryptosporidiosis in the first three weeks of life. Similar results are described in lambs, also a susceptible species to cryptosporidia. These studies suggest a long-term negative effect of cryptosporidia on growth performance and production efficiency.

Here’s how you can support your calves against cryptosporidia

High resistance of the pathogens to environmental influences, a very low necessary infection dose combined with an elevated excretion of infectious oocysts, and the possibility of autoinfection make cryptosporidia tough opponents. This is also reflected in their worldwide distribution.

What is the treatment?

Suitable drugs for the treatment of cryptosporidiosis are currently unavailable on the market. The only medicine that can be used in case of cryptosporidiosis infestation may only be administered to calves that have had diarrhea symptoms for 24 hours or less. Accordingly, this agent is usually used only for prevention. Scientific studies on its effectiveness are contradictory; some suggest that it merely delays the onset of the disease. In addition, it is not always easy to use due to the exact dosage that must be followed. Doubling the dose (sometimes happening already due to incorrectly observed intervals between doses) can lead to a toxic overdose.

Accordingly, only the symptoms of the disease – diarrhea with its accompanying symptoms – can be treated. Electrolyte and water losses must be continuously compensated with the help of a high-quality electrolyte drink. The buffer substances contained also reduce the hyperacidity of the blood caused by faulty fermentation in the intestines. For successful treatment, the electrolyte drink should be given in addition to the milk drink. Under no circumstances should the feeding of milk or milk replacer be discontinued because the sick calf urgently needs energy and nutrients. Opinions to the contrary are outdated.

As always: prevention is better than treatment

To make it more difficult for cryptosporidiosis to spread from the outset, it is worth looking at the risk factors. These include direct contact with other calves and general herd size. Furthermore, organic farms seem to have more problems with cryptosporidia. Weather also influences calves born during warmer and, at the same time, wetter weather periods (temperature-humidity index) often get sick.

Due to the limited possibilities for treatment, prevention is of greater importance. For other diarrheal pathogens such as rotavirus, coronavirus, and *E. coli*, it has become established practice to vaccinate dams to achieve better passive immunization of the calf. However, commercial vaccination against cryptosporidia is not currently available, making dam vaccination as unavailable as calf vaccination.

Accordingly, optimal colostrum management is the first way to protect the calf from cryptosporidia infection. This also confirms the general discussion on the Failure of Passive Transfer: various studies suggest that calves with poor immunoglobulin supply suffer from diarrhea more frequently than calves with good supply, although a concrete link to cryptosporidia itself cannot always be established with certainty.

Furthermore, it is essential to break the chain of infection within farms. In addition to the separate housing of the calves, it is necessary to ensure consistent hygiene. One should take advantage of the pathogen's weakness as well as its sensitivity to high temperatures and ensure that the water temperature is sufficiently high when cleaning the calf pens and calving area. When disinfecting afterward, it is crucial to consider the spectrum of activity of the agent used, as not all are effective against cryptosporidia.

Egg immunoglobulins support animals against cryptosporidia

Egg immunoglobulins were initially designed to help chicks get started. In this process, hens form antibodies against pathogens they are confronted with. As studies have shown, this also works with cryptosporidia. Cama and Sterling (1991) tested their produced antibodies in the neonatal mouse model and achieved a significant ($P \leq 0.001$) reduction in parasites there. Kobayashi et al. (2004) registered decreased binding of sporozoites to the intestinal cell model and their decreased viability in addition to oocyst reduction.

In the IRIG Research Institute (2009, unpublished), feeding egg powder with immunoglobulins against cryptosporidia (10 g/day) to 15 calves reduced oocyst excretion. Before administration, calves excreted an average of 106.42 oocysts/g of feces. After administration of egg powder, only two calves still showed 103.21 oocysts/g feces, and the other 13 of the 15 calves showed no oocyst excretion. All these results are confirmed by positive customer feedback on IgY-based feed supplements.

Egg immunoglobulins and optimal colostrum management as a key solution

Since there are no effective drugs against cryptosporidia, animals must be prophylactically protected against this disease as much as possible. In addition to optimal colostrum management, which means feeding high-quality colostrum (IgG≥50g/L) to the calf as soon as possible after birth, we have products with egg immunoglobulins available to support the calf as a prophylactic against cryptosporidia infestation and thus prevent significant performance losses, especially during rearing.

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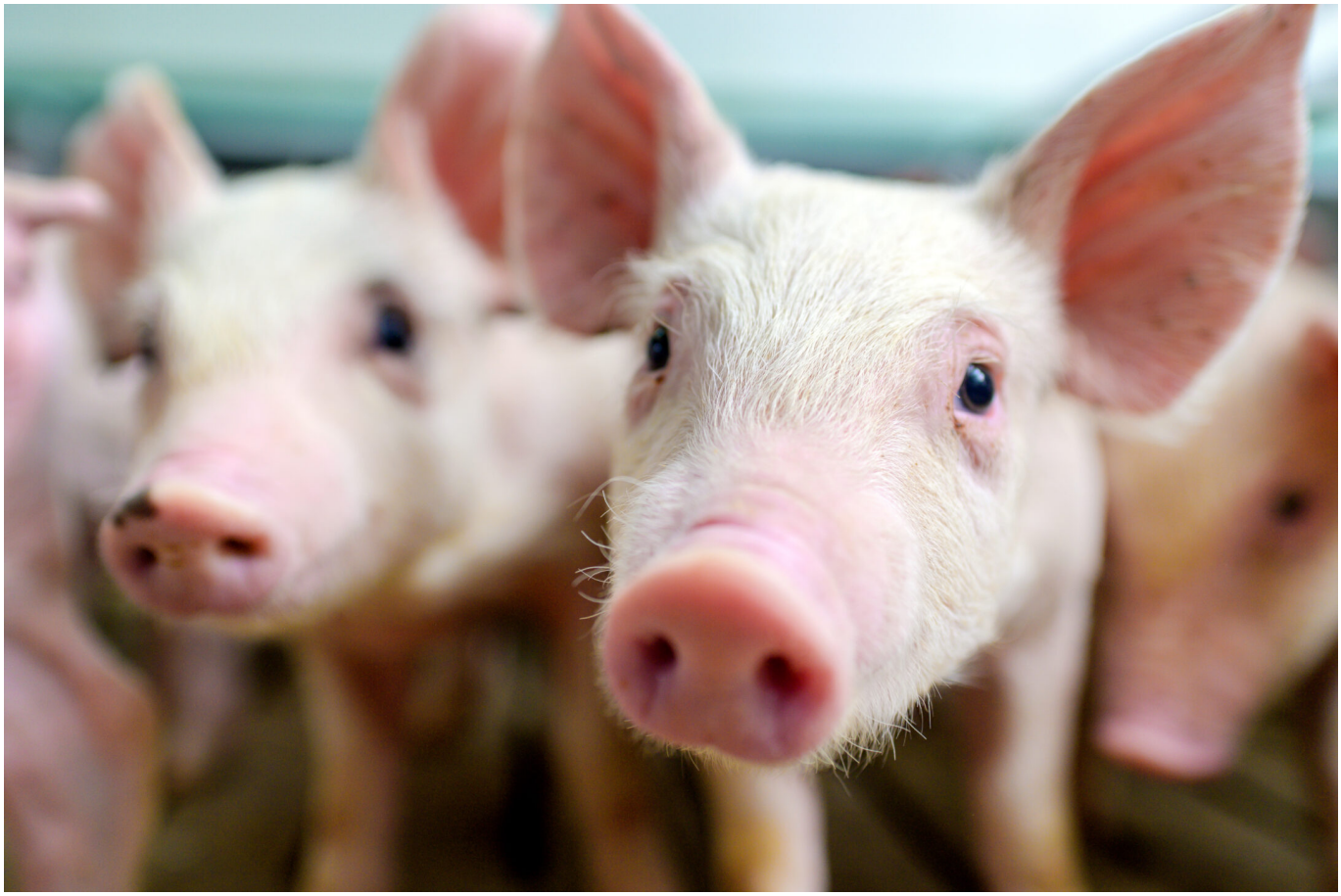
Piglet Nutrition Scenarios for AGP Removal



Over the past 60 years, antibiotics have played an essential role in the swine industry as a tool that swine producers rely on to control diseases and to reduce mortality. Besides, antibiotics are also known to improve performance, even when used in subtherapeutic doses. The perceived overuse of antibiotics in pig production, especially as growth promoters (AGP), have raised concerns from governments and public opinion, regarding the emergence of multidrug-resistant bacteria, adding a threat not only to animal but also human health. The challenges raised regarding AGPs and the need for their reduction in livestock led to the development of combined strategies such as the "One Health Approach", where animal health, human health, and the environment are interlaced and must be considered in any animal production system.

In this scenario of intense changes, swine producers must evaluate strategies to adapt their production systems to accomplish the global pressure to reduce antibiotics and still have a profitable operation.

Many of these concerns focus on piglet nutrition, since the use of sub-therapeutic levels of antimicrobials as growth promotors is still a regular practice for preventing post-weaning diarrhea in many countries (Heo

et al., 2013; Waititu et al., 2015). Taking that into consideration, this article serves as a practical guide to swine producers through AGP removal and its impacts on piglet performance and nutrition Three crucial points will be addressed:

1. Why is AGP removal a global trend?
2. What are the major consequences for piglet nutrition and performance?
3. What alternatives do we have to guarantee optimum piglet performance in this scenario?

AGP removal: a global issue

Discussions on the future of the swine industry include understanding how and why AGP removal became such important topic worldwide. Historically, European countries have led discussions on eliminating AGP from livestock production. In Sweden, AGPs were banned from their farms as early as 1986. This move culminated into a total ban of AGPs in the European Union in 2006. Other countries followed same steps. In Korea, AGPs were removed from livestock operations in 2011. The USA is also putting efforts into limiting AGPs and the use of antibiotics in pig farms, as published in guidance revised by the Food and Drug Administration (FDA, 2019). In 2016, Brazil and China banned Colistin, and the Brazilian government also announced the removal of Tylosin, Tiamulin, and Lincomycin in 2020. Moreover, countries like India, Vietnam, Bangladesh, Buthan, and Indonesia have announced strategies for AGP restrictions (Cardinal et al., 2019; Davies and Walsh, 2018).

The major argument against AGPs and antibiotics in general is the already mentioned risk of the development of antimicrobial resistance, limiting the available tools to control and prevent diseases in human health. This point is substantiated by the fact that resistant pathogens are not static and exclusive to livestock, but can also spread to human beings (Barbosa and Bünzen, 2021). Moreover, concerns have been raised in regard to the fact that antibiotics in pig production are also used by humans – mainly third-generation antibiotics. The pressure on pig producers increased and it is today multifactorial: from official regulatory departments and stakeholders at different levels, who need to consider public concerns about antimicrobial resistance and its impact on livestock, human health, and the sustainability of farm operations (Stein, 2002).

It is evident that the process of reducing or banning antibiotics and AGPs in pig production is already a global issue and increasing as it takes on new dimensions. As Cardinal et al. (2019) suggest, that process is irreversible. Companies that want to access the global pork market and comply with increasingly stricter regulations on AGPs must re-invent their practices. This, however, is nothing new for the pig industry. For example, pig producers from the US and Brazil have adapted their operations in order to not use ractopamine to meet the requirements from the European and Asian markets. We can be sure, therefore, that the global pig industry will find a way to replace antibiotics.

With that in mind, the next step is to evaluate the consequences of AGP withdrawal from pig diets and how that affects the animals' overall performance.

Consequences in piglet health and performance

Swine producers know very well that weaning pigs is challenging. Piglets are exposed to many biological stressors during that transitioning period, including introducing the piglets to new feed composition (going from milk to plant-based diets), abrupt separation from the sow, transportation and handling, exposure to new social interactions, and environmental adaptations, to name a few. Such stressors and physiological challenges can negatively impact health, growth performance, and feed intake due to immune systems dysfunctions (Campbell et al. 2013). Antibiotics have been a very powerful tool to mitigate this performance drop. The question then is, how difficult can this process become when AGPs are removed entirely?

Many farmers around the world still depend on AGPs to make the weaning period less stressful for piglets. One main benefit is that antibiotics will reduce the incidence of PWD, with subsequent improved growth performance (Long et al., 2018). The weaning process can create ideal conditions for the overgrowth of pathogens, as the piglets' immune system is not completely developed and therefore not able to fight back. Those pathogens present in the gastrointestinal tract can lead to post-weaning diarrhea (PWD), among many other clinical diseases (Han et al., 2021). PWD is caused by *Escherichia coli* and is a global issue in the swine industry, as it compromises feed intake and growth performance throughout the pig's life, also being a common cause for losses due to young pig death (Zimmerman, 2019).

Cardinal et al. (2021) also highlight that the hypothesis of a reduced intestinal inflammatory response is one explanation for the positive relationship between the use of AGPs and piglet weight gain. Pluske et al. (2018) point out that overstimulation of the immune system can negatively affect pig growth rate and feed use efficiency. The process is physiologically expensive in terms of energy and also can cause excessive prostaglandin E2 (PGE2) production, leading to fever, anorexia, and reduction in pig performance. For instance, Mazutti et al. (2016) showed an increased weight gain of up to 1.74 kg per pig in animals that received colistin or tylosin in sub-therapeutic levels throughout the nursery. Helm et al. (2019) found that pigs medicated with chlortetracycline in sub-therapeutic levels increased average daily gain in 0.110 kg/day. Both attribute the higher weight to the decreased costs of immune activation determined by the action of AGPs on intestinal microflora.

On the other hand, although AGPs are an alternative for controlling bacterial diseases, they have also proved to be potentially deleterious to the beneficial microbiota and have long-lasting effects caused by microbial dysbiosis – abundance of potential pathogens, such as *Escherichia* and *Clostridium;* and a reduction of beneficial bacteria, such as *Bacteroides*, *Bifidobacterium,* and *Lactobacillus* (Guevarra et al., 2019; Correa-Fiz, 2019). Furthermore, AGPs reduced microbiota diversity, which was accompanied by general health worsening in the piglets (Correa-Fiz, 2019).

It is also important to highlight that the abrupt stress caused by suckling to weaning transition has consequences in diverse aspects of the function and structure of the intestine, which includes crypt hyperplasia, villous atrophy, intestinal inflammation, and lower activities of epithelial brush border enzyme (Jiang et al., 2019). Also, the movement of bacteria from the gut to the body can occur when the intestinal barrier function is deteriorated, which results in severe diarrhea and growth retardation. Therefore, nutrition and management strategies during that period are critical, and key gut nutrients must be used to support gut function and growth performance.

With all of that, it is more than never necessary to better understand the intestinal composition of young pigs and finding strategies to promote gut health are critical measures for preventing the overgrowth and colonization of opportunistic pathogens, and therefore being able to replace AGPs (Castillo et al., 2007).

Viable alternatives for protecting the piglets

The good news is that the swine industry already has effective alternatives that can replace AGP products and guarantee good animal performance.

Immunoglobulins from egg yolk (IgY) have proven to be a successful alternative to weaned piglet nutrition. Investigations have shown that egg antibodies improve the piglets' gut microbiota, making it more stable (Han et al., 2021). Moreover, IgY optimizes piglet immunity and performance while reducing occurrences of diarrhea caused by *E. coli*, rotavirus, and *Salmonella sp.* (Li et al., 2016).

Phytomolecules (PM) are also potential alternatives for AGP removal, as they are bioactive compounds with antibacterial, antioxidant, and anti-inflammatory characteristics (Damjanović-Vratnica et al., 2011; Lee and Shibamoto, 2001). When used for piglet diet supplementation, phytomolecules optimize intestinal health and improve growth performance (Zhai et al., 2018).

Han et al. (2021) evaluated a combination of IgY (Globigen® Jump Start, EW Nutrition) and phytomolecules (Activo®, EW Nutrition) supplementation in weaned piglets' diets. Results from that study (Table 1 and 2) showed that this strategy decreases the incidence of PWD and coliforms, increases feed intake, and

improves the intestinal morphology of weaned pigs, making that combination a viable AGP replacement.

Items	Dietary Treatments [1]				SEM [2]	*p*-Value
	NC	PC	AGP	IPM		
Body weight, kg						
Initial	7.29	7.27	7.30	7.31	0.01	0.174
Day 17	9.57	9.42	9.77	9.80	0.07	0.131
Day 42	20.41	19.77	20.46	20.56	0.17	0.372
Days 1–17						
ADFI [3], g	293.23	281.55	275.52	275.52	3.61	0.267
ADG [3], g	142.58	133.92	154.04	155.47	4.04	0.192
F:G [3]	2.10 [a]	2.13 [a]	1.82 [b]	1.78 [b]	0.05	0.005
Days 18–42						
ADFI, g	731.25	705.60	706.83	721.64	8.65	0.697
ADG, g	416.73	396.92	413.36	411.16	5.22	0.574
F:G	1.76	1.78	1.72	1.76	0.02	0.595
Days 1–42						
ADFI, g	564.39	544.06	542.52	551.69	5.86	0.557
ADG, g	312.29	296.73	314.57	313.75	3.87	0.321
F:G	1.81 [a,b]	1.84 [a]	1.73 [b]	1.76 [a,b]	0.02	0.098

[a,b] Different superscript letters within a row indicate significant difference between groups ($p < 0.05$). [1] Dietary treatments were as follows: NC, negative control group, basal diet; PC, positive control group, basal diet, and challenged with *E. coli* K88; AGP, antibiotic growth promoter group, basal diet supplemented with 75 mg/kg chlortetracycline, 50 mg/kg oxytetracycline calcium, and 40 mg/kg zinc bacitracin, and challenged with *E. coli* K88; IPM, IgY and PM group, basal diet supplemented with IgY at dose of 2.5 g/kg and 1 g/kg and PM at dose of 300 mg/kg and 150 mg/kg during days 1 to 17 and 18 to 42, respectively, and challenge with *E. coli* K88. [2] SEM, standard error of the mean, $n = 8$. [3] ADFI, average daily feed intake; ADG, average daily gain; F:G, ratio of feed to weight gain.

Table 1. Effect of dietary treatments on the growth performance of weaned pigs challenged with E. coli K88 (SOURCE: Han et al., 2021).

Items [3]	Dietary treatments [1]				SEM [2]	*p*-Value
	NC	PC	AGP	IPM		
Day 1–6 b.c.	5.56	5.55	3.47	5.20	0.67	0.335
Day 7–9 c.t.	16.67 [c]	45.23 [a]	23.61 [b,c]	30.55 [b]	2.65	<0.001
Day 1–7 p.c.	25.30 [c]	60.88 [a]	40.21 [a,b]	38.09 [b]	2.48	<0.001
Day 8–17 p.c.	18.05	26.00	18.81	22.50	1.37	0.061
Day 18–33 p.c.	15.62	21.00	15.41	18.96	1.49	0.247

[a–c] Different superscript letters within a row indicate significant difference between groups ($p < 0.05$). [1] Dietary treatments were as follows: NC, negative control group, basal diet; PC, positive control group, basal diet, and challenged with *E. coli* K88; AGP, antibiotic growth promoter group, basal diet supplemented with 75 mg/kg chlortetracycline, 50 mg/kg oxytetracycline calcium, and 40 mg/kg zinc bacitracin, and challenged with *E. coli* K88; IPM, IgY and PM group, basal diet supplemented with IgY at dose of 2.5 g/kg and 1 g/kg and PM at dose of 300 mg/kg and 150 mg/kg during days 1 to 17 and 18 to 42, respectively, and challenge with *E. coli* K88. [2] SEM, standard error of the mean, $n = 8$. [3] Items: Day 1–6 b.c., days 1–6 before-chanllenging with *E. coli* K88; Day 7–9 c.t., days 7–9 challenging time of experiment; Days 1–7 p.c., days1–7 post-challenging with *E. coli* K88.

Table 2. Effect of dietary treatments on the post-weaning diarrhea incidence of weaned pigs challenged with E. coli K88 (%) (SOURCE: Han et al., 2021).

A trial conducted at the Institute of Animal Sciences of the Chinese Academy of Agricultural Sciences, China, supplemented weaning pigs challenged by E. coli K88 with a combination of PM (Activo®, EW Nutrition) and IgY (Globigen® Jump Start). The trial reported that this combination (AC/GJS) showed fewer diarrhea occurrences than in animals from the positive group (PC) during the first week after the challenge and similar diarrhea incidence to the AGP group during the 7th and 17th days after challenge (Figure 1).

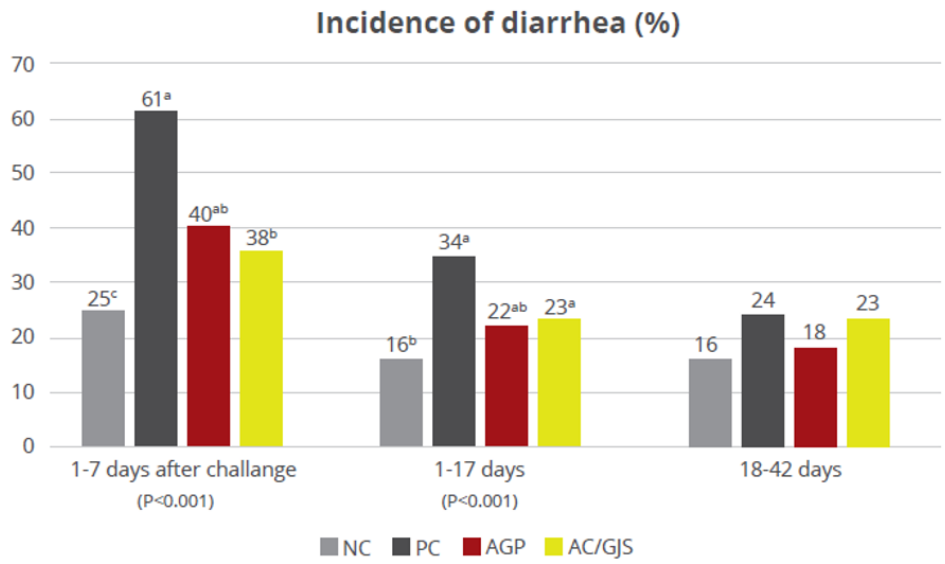


Figure 1 – Incidence of diarrhea (%). NC: negative group, PC: positive group, AGP: supplementation with AGP, AC/GJS: combination of PM (Activo, EW Nutrition) and IgY (Globigen Jump Start).

The same trial also showed that the combination of these non-antibiotic additives was as efficient as the AGPs in improving pig performance under bacterial enteric challenges, showing positive effects on body weight, average daily gain (Figure 2), and feed conversion rate (Figure 3).

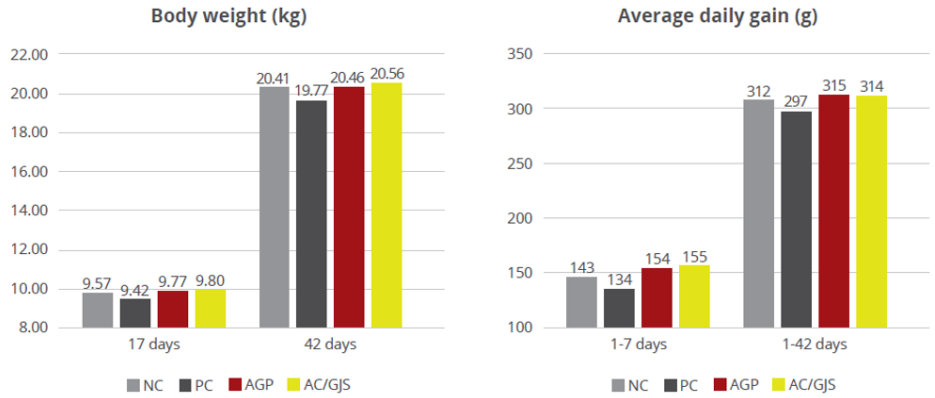


Figure 2 – Body weight (kg) and average daily gain (g). NC: negative group, PC: positive group, AGP: supplementation with AGP, AC/GJS: combination of PM (Activo, EW Nutrition) and IgY (Globigen Jump Start).

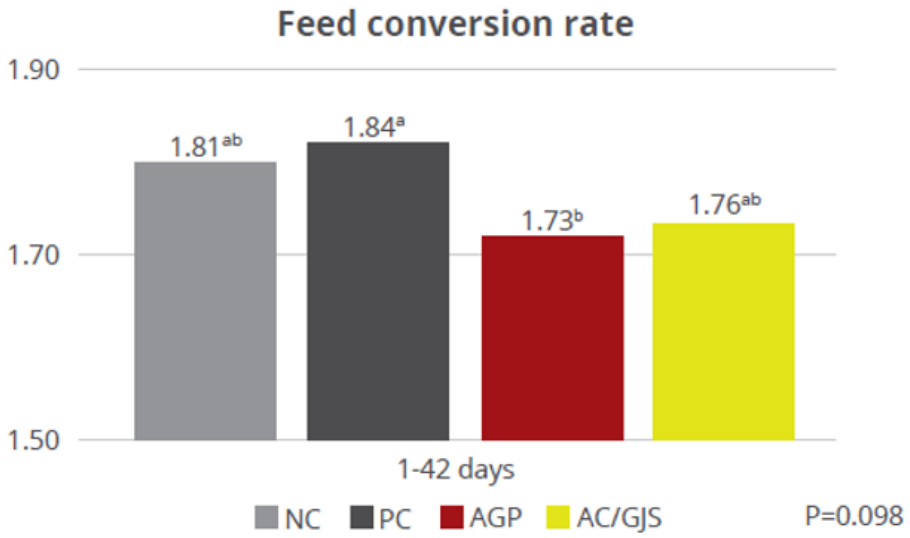


Figure 3 – Feed conversion rate. NC: negative group, PC: positive group, AGP: supplementation with AGP, AC/GJS: combination of PM (Activo, EW Nutrition) and IgY (Globigen Jump Start).

The multiple benefits of using IgY in piglet nutrition strategies are also highlighted by Rosa et al. (2015), Figure 4, and Prudius (2021).

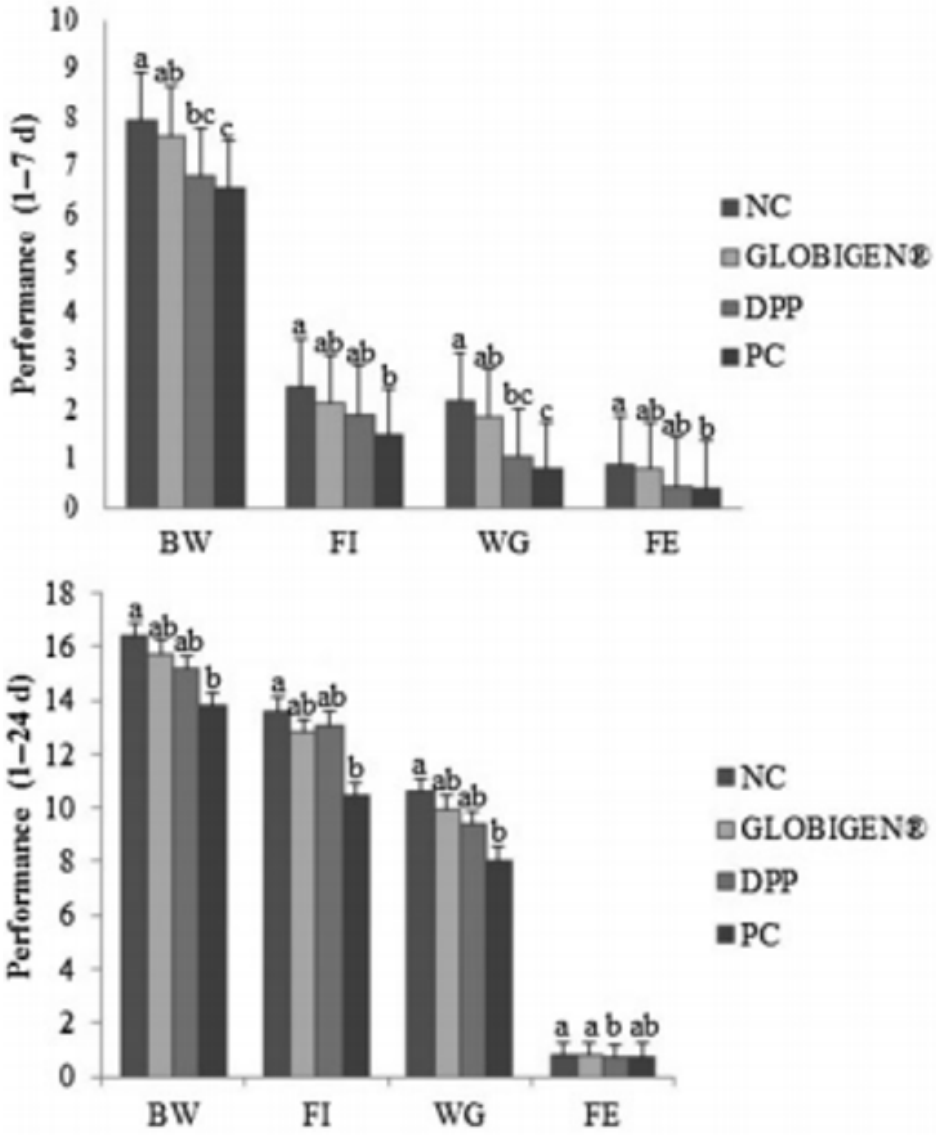


Figure 4. Effect of treatments on the performance of newly weaned piglets. Means (±SEM) followed by letters a,b,c in the same group of columns differ ($p < 0.05$). NC (not challenged with ETEC, and diet with 40 ppm of colistin, 2300 ppm of zinc, and 150 ppm of copper). Treatments challenged with ETEC: GLOBIGEN® (0.2% of GLOBIGEN®); DPP (4% of dry porcine plasma); and PC (basal diet) (SOURCE: Rosa et al., 2015).

Conclusions

AGP removal and overall antibiotic reduction seems to be the only direction that the global swine industry must take for the future. From the front line, swine producers demand cost-effective AGP-free products that don't compromise growth performance and animal health. Along with this demand, finding the best strategies for piglet nutrition in this scenario is critical in minimizing the adverse effects of weaning stress. With that in mind, alternatives such as egg immunoglobulins and phytomolecules are commercial options that are already showing great results and benefits, helping swine producers to go a step further into the future of swine nutrition.

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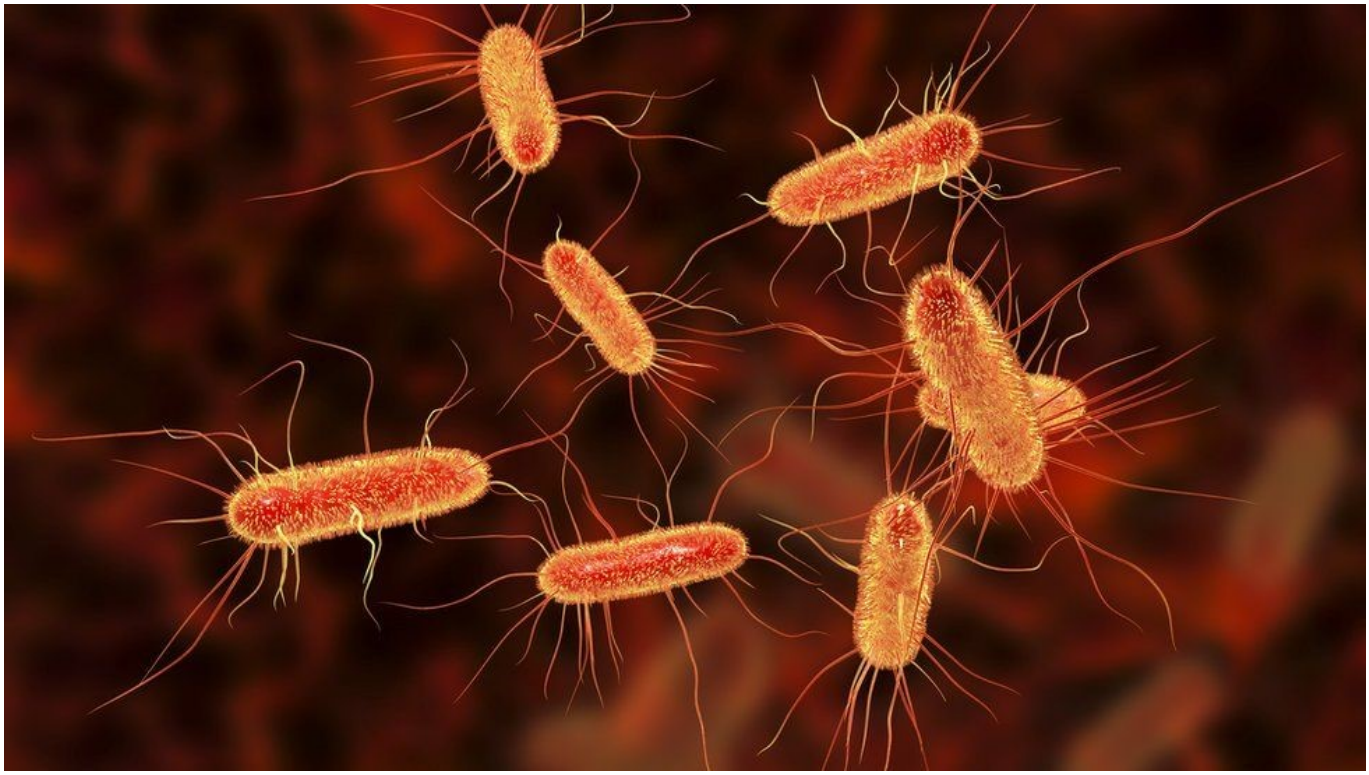
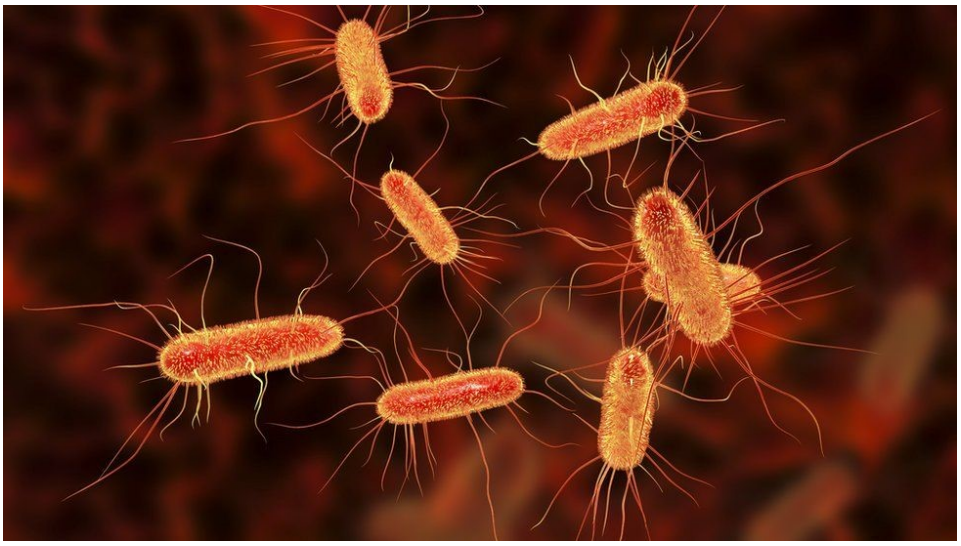
The hidden danger of endotoxins in animal production



Find out more about endotoxins here

Find out why LPS can cause endotoxemia and how intelligent toxin mitigation solutions can support endotoxin management.



Each E. coli bacterium contains about 100 lipopolysaccharides molecules in its outer membrane

Lipopolysaccharides (LPS) are the major building blocks of the outer walls of Gram-negative bacteria. Throughout its life cycle, a bacterium releases these molecules, which are also known as endotoxins, upon cell death and lysis. The quantity of LPS present in Gram-negative bacteria varies between species and serotypes; *Escherichia coli*, for example, contain about 100 LPS/bacterial cell. When these are released into the intestinal lumen of chickens or swine, or in the rumen of polygastric animals, they can cause serious damage to the animal's health and performance by over-stimulating their immune system.

How lipopolysaccharides cause disease

LPS are rather large and structured chemical molecules with a weight of over 100,000 D. They are highly thermostable; boiling in water at 100°C for 30 minutes does not destabilize their structure. LPS consist of three chemically distinct sections: a) the innermost part, lipid A, consisting mostly of fatty acids; b) the core, which contains an oligosaccharide; and c) the outer section, a chain of polysaccharides called O-antigen (Figure 1).

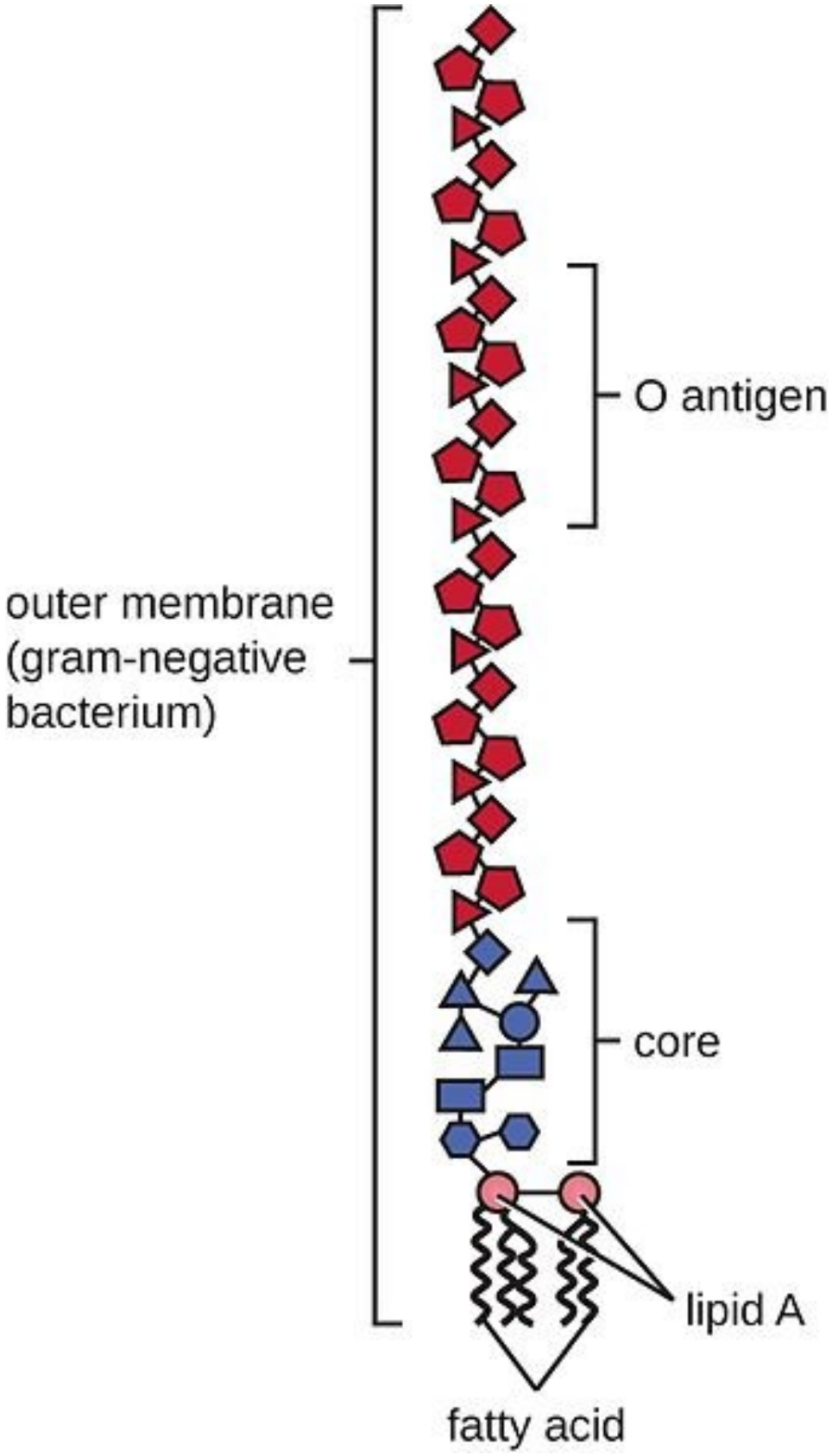


Figure 1: Structure of an LPS

The toxicity of LPS is mainly caused by lipid A; however, both lipid A and O-antigen stimulate the immune system. This happens when the LPS pass the mucosa and enter the bloodstream or when they attack the leukocytes.

The intestinal mucosa is the physical immune barrier that protects the microvilli from external agents (bacteria, free LPS viruses, etc.). Despite its strength (the thickness, for example, amounts to ≈830 µm in

the colon and ≈123 µm in the jejunum), vulnerable points exist (cf. Zachary 2017).

LPS can easily come into contact with the cells of the *lamina propria* (a layer of connective tissue underneath the epithelium) through the microfold (M) cells of the Peyer's patches (which consist of gut-associated lymphoid tissue). The M cells are not covered by mucus and thus exposed.

Secondly, LPS can also pass through the mucosa, where they become entangled in this gelatinous structure. There, they come into contact with the lymphocytes or can reach the regional lymph nodes through the afferent lymphatic vessels.

Thirdly, LPS might affect the tight junctions, the multiprotein complexes that keep the enterocytes (cells that form the intestinal villi) cohesive. By destabilizing the protein structures and triggering enzymatic reactions that chemically degrade them, LPS can break the tight junctions, reaching the first capillaries and, consequently, the bloodstream.

The presence of endotoxins in the blood, endotoxemia, can trigger problematic immune responses in animals. An innate immune stimulation leads to an increase in the concentration of pro-inflammatory cytokines in the blood and, consequently, to an induced febrile response in the animal: heat production increases, while the available metabolic energy decreases. As a result, performance suffers, and in the worst-case scenario, septic shock sets in. Furthermore, when LPS compromise intestinal integrity, the risk of secondary infections increases, and production performance may decline.

LPS' modes of action

How does all of this happen? The physiological consequences of endotoxemia are quite complex. Simplified, the immune system response to LPS in the blood takes three forms:

- The stimulation of **TLR4** (toll-like receptor 4) induces monocytes and macrophages to secrete critical pro-inflammatory cytokines, primarily interleukin (IL) IL-1β, IL-6, IL-8, and tumor necrotic factor (TNF) α and β. TLR4 is a structure on the cell membrane of mainly macrophages and leukocytes, which is activated by the LPS-binding protein (LBP).
- The **complement cascade** constitutes about 10% of plasma proteins and determines the chemotaxis and activation of leukocytes. It can form a membrane attack complex (MAC), which perforates the membranes of pathogenic cells, enabling lysis.
- The **Hagemann factor**, also known as coagulation factor XII: once stimulated by LPS, it initiates the formation of fibrin (through the intrinsic coagulation pathway), which might lead to thrombosis. The Hagemann factor directly stimulates the transformation of prekallikrein to kallikrein (enzymes involved in regulating blood pressure).

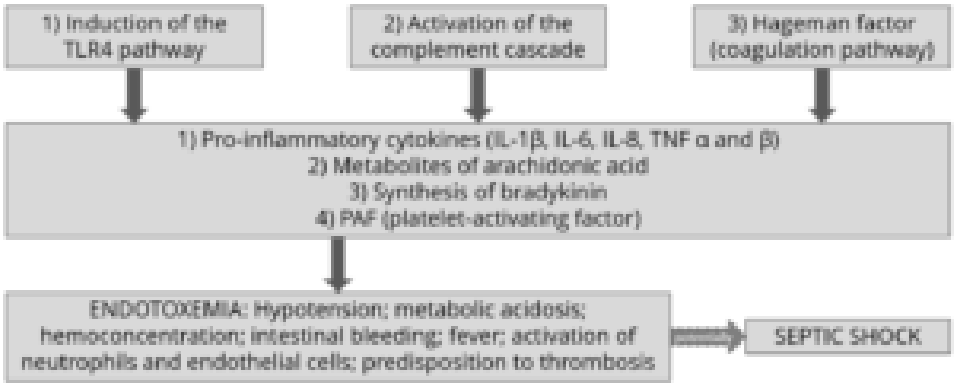


Figure 2: How LPS leads to endotoxemia – 3 modes of action

These three modes of action of inflammatory stimulation lead to important physiological reactions:

- **Pro-inflammatory cytokines** (see above) modulate the functional expression of other immune cell types during the inflammatory response;
- **Metabolites of arachidonic acid** (prostaglandins, leukotrienes, and lipoxins), intra- and extracellular messengers that influence the coagulation cascade;

- Synthesis in the blood of **bradykinin**, a peptide responsible for the typical symptoms of inflammation, such as swelling, redness, heat and pain;
- **PAF** (platelet-activating factor), which creates inflammatory effects through narrowing of the blood vessels and constriction of the airways, but also through the degranulation of leukocytes.

The symptoms of endotoxemia are: hypotension, metabolic acidosis, hemoconcentration, intestinal hemorrhage, fever, activations of neutrophils and endothelial cells, and predisposition to thrombosis.

In case of a progression to septic shock, the following sequence takes place:

1) Reduction in blood pressure and increased heart rate (hemodynamic alterations)

2) Abnormalities in body temperature

3) Progressive hypoperfusion at the level of the microvascular system

4) Hypoxic damage to susceptible cells

Up to here, symptoms follow a (severe) endotoxemia pathogenesis. A septic shock furthermore entails:

5) Quantitative changes in blood levels of leukocytes and platelets

6) Disseminated intravascular coagulation (see Hageman factor)

7) Multi-organ failure

8) Death of animal

If an animal is continously challenged with endotoxins, experiences septic shock, or comes close to it, it risks developing LPS tolerance, also known as CARS (compensatory anti-inflammatory response syndrome). This syndrome essentially depresses the immune system to control its activity. The anti-inflammatory prerogative of CARS is not to interfere directly with the elimination of pathogens but to regulate the “excessive” inflammatory reaction in a hemostatic way. However, this regulation can be extremely dangerous as the syndrome involves a lack of homeostasis control, and an excessive depression of the immune system leaves the organism exposed to the actual pathogens.

Farm animal research on endotoxemia pathogenesis

Lipopolysaccharides are difficult to quantify in the intestine of a live animal. One way to evaluate a possible endotoxemia is to analyze biomarkers present in the bloodstream. The most important one is the LPS themselves, which can be detected in a blood sample taken from the animal via ELISA. Other biomarkers include pro-inflammatory interleukins, such as TNF α and β, IL-6 or IL-8, and fibrin and fibrinogen (though they are not specific to endotoxemia). It is vital to carry out a blood sample analysis to deduce a possible endotoxemia from symptoms and performance losses in the animal.

How the metabolic effects of endotoxemia depress performance

One of the biggest issues caused by endotoxemia is that animals reduce their feed intake and show a poor feed conversion rate (FCR). Why does this happen? The productive performance of farm animals (producing milk, eggs, or meat) requires energy. An animal also requires a certain baseline amount of energy for maintenance, that is, for all activities related to its survival. As a result of inflammation and all those physiological reactions mentioned above, endotoxemia leads to a feverish state. Maintenance needs

to continue; hence, the energy required for producing heat will be diverted from the energy usually spent on producing milk, egg, meat, etc., and performance suffers.

The inflammation response can result in mitochondrial injury to the intestinal cells, which alter the cellular energy metabolism. This is reflected in changes to the levels in adenosine triphosphate (ATP), the energy "currency" of living cells. A study by Li et al. (2015) observed a respective reduction of 15% and 55% in the ATP levels of the jejunum and ileum of LPS-challenged broilers, compared to the unchallenged control group. This illustrates the extent to which animals lose energy while they experience (more or less severe) endotoxemia.

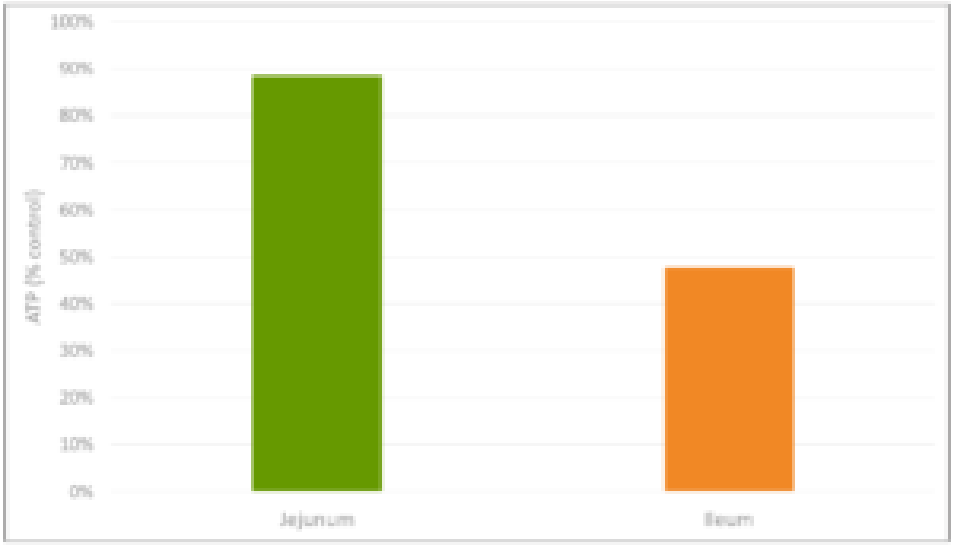


Figure 3: Reduction in ATP level in Jejunum and Ileum in broilers (adapted from Li et al., 2015)

A piglet study by Huntley, Nyachoti, and Patience (2017) took this idea further (Figure 4): 3 groups of 10 Yorkshire x Landrace pigs, weighing between 11 and 25 kg, were studied in metabolic cages and in respiratory chambers. This methodology allows for simultaneous measurement of oxygen consumption, CO_2 production, energy expenditure, physical activity, and feed/water intake. The study found that LPS-challenged pigs retained 15% less of the available metabolizable energy and showed 25% less nutrient deposition. These results show concrete metabolic consequences caused by the febrile response to endotoxemia we discussed above.

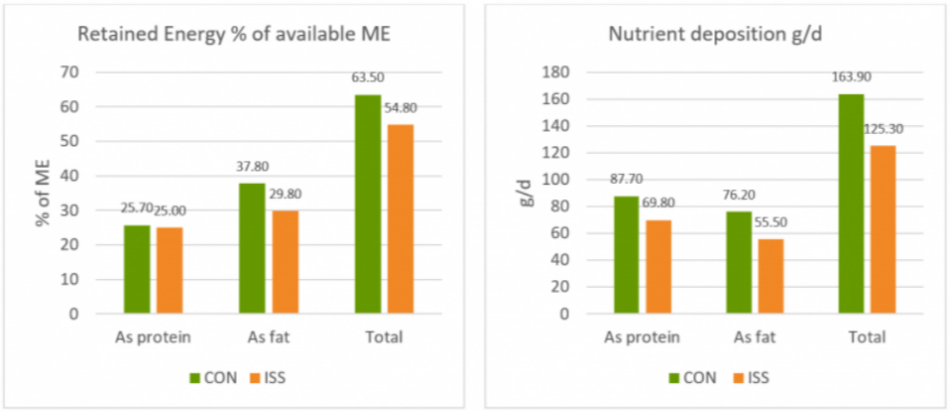


Figure 4: Retained Energy as % of ME intake and nutrient deposition of pigs in metabolic cages (adapted from Huntley, Nyachoti, and Patience, 2017)

Control treatment (CON) = Pigs fed by a basal diet
Immune system stimulation treatment (ISS) = Pigs given LPS (E. coli serotype 055:B5) injection

A loss of energy retained due to a reduction in available metabolizable energy leads to losses in performance as the amount of energy available for muscle production and fat storage will be lower. Furthermore, the decrease in feed intake creates a further energy deficit concerning production needs.

A trial carried out at the University of Illinois examined the effects of repeated injections of 400 µg *E. coli* LPS on chick performance from 11 to 22 days after hatching. The chicks were fed casein-based diets with graded levels of arginine. LPS administration reduced weight gain ($P<0.05$) and feed intake, and these effects tended to be worse at higher levels of arginine supplementation (Figure 5). The researchers hypothesize that, in response to endotoxin and elevated cytokine levels, macrophages use more arginine to produce nitric oxide, diverting it from protein production for muscle development.

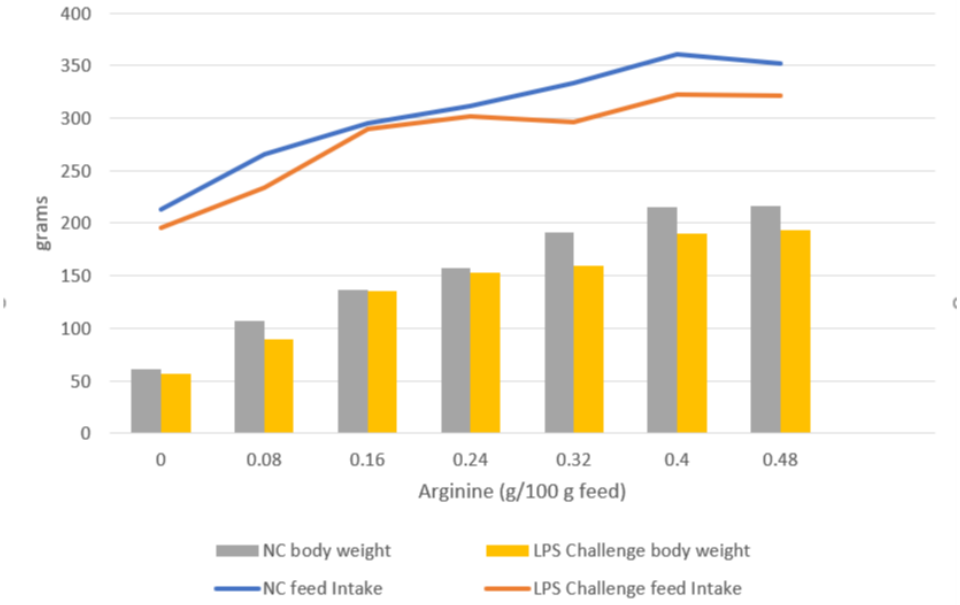


Figure 5: Effects of LPS on feed intake and body weight gain in chicks fed graded level of arginine (based on Webel, Johnson, and Baker, 1998)

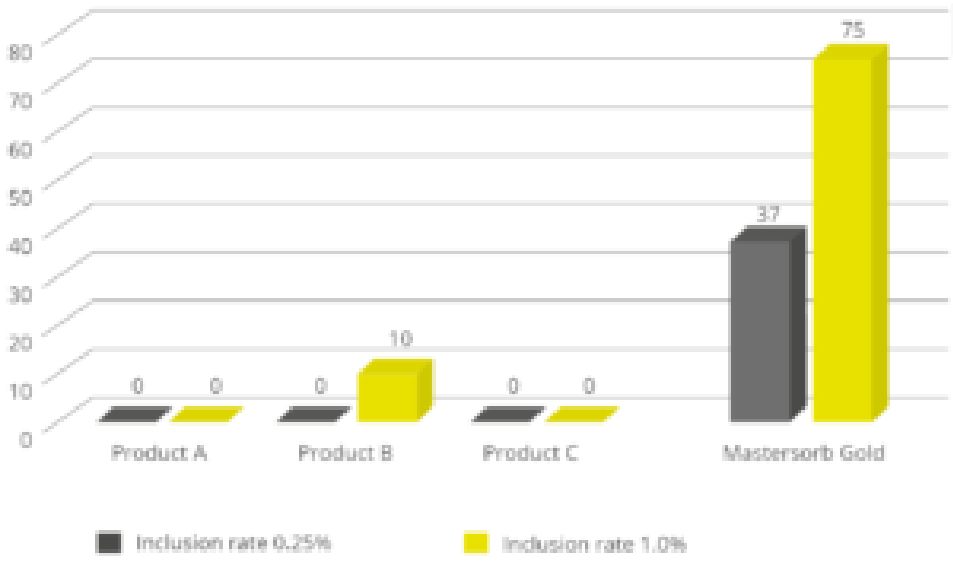
NC = negative control

This data on poultry complements the results for swine, again showing that endotoxin-induced energy losses quantifiably depress animal performance even in milder disease cases.

The way forward: Endotoxin mitigation

Animals suffering from endotoxemia are subject to severe metabolic dysfunctions. If they do not perish from septic shock, they are still likely to show performance losses. Moreover, they at great risk of immunosuppression caused by the immune system “overdrive.” Effective endotoxin mitigating agents can help to prevent these scenarios.

EW Nutrition’s Mastersecure Gold is not only a leading anti-mycotoxin agent; thanks to its specific components, it effectively binds bacterial toxins. An *in vitro* study conducted at the Hogeschool Utrecht laboratory (part of Utrecht University) evaluated the binding capacity of Mastersecure Gold on LPS compared to three different competitor products. All products were tested at two different inclusion rates. At an inclusion rate of 0.25%, only Mastersecure Gold reduced the toxin load on the solution by 37%. At 1% inclusion, Mastersecure Gold (noted as Mastersorb below) bound 75% of the toxin, while only one competitor product demonstrated any binding (10%).



Lipopolysaccharides are a constant challenge for animal production. The quantity of Gram-negative bacteria in an animal intestine is considerable; therefore, the danger of immune system over-stimulation through endotoxins cannot be taken lightly. Producers need to prioritize the maintenance of intestinal eubiosis in production animals proactively; for instance, through targeted gut health-enhancing additives based on phytomolecules and, possibly, organic acids.

Most importantly, the detrimental impact of LPS can be mitigated by using a high-performance agent such as Mastersecure Gold. To limit losses from an energy point of view yields positive results in terms of production levels and the prevention of secondary infections, preserving animal health and farms' economic viability.

By Claudio Campanelli, EW Nutrition

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